AMENDMENTS TO THE SPECIFICATION

Please **replace** paragraph [00010] at pages 5-6 with the following paragraph:

[00010] Known crystal structures of protein kinases reveals that they share very similar fold and topology and are structurally homologous. This is true even though the amino acid sequences of protein kinases may be very divergent, i.e., low sequence ~~homologly~~ homology or identity.

Please **replace** paragraph [00040] at page 23 with the following paragraph:

[00040] The preparation of the chimeric protein kinase may be achieved by methods well known to those of skill in the art. For example, the inhibitor ~~biding~~ binding site amino acids of the second protein kinase may be substituted with the inhibitor binding site amino acids of the first protein kinase using site-directed mutagenesis, PCR, or other methods of altering the DNA, or a cDNA encoding the second protein kinase. The chimeric protein kinase may then be expressed by conventional recombinant DNA techniques (may be expressed in prokaryotic and/or eukaryotic cells, such as bacteria, yeast or insect cells, as described further below) and may be purified using conventional chromatography, including ion exchange, gel filtration, affinity chromatography.

Please **replace** paragraph [00059] at page 34 with the following paragraph:

[00059] p38 crystals were obtained as previously described. *See* Wang et al., ~~*J. Biol. Chem.* 6:1117-128 (1998)~~ *Proc. Natl. Acad. Sci. U.S.A.*, 94:2327-32 (1997). Purified rat p38α

alternative splice form~~, NCBI data base entry AAK1541~~, (SEQ ID NO:40) was used to grow the crystals.

Please **replace** paragraph [0061] at pages 34-35 with the following paragraph:

[0061] The structures of the p38 crystals soaked in either sulindac sulfide or PD98059 were solved using better than [[2.7X]] 2.7Å resolution data and the structures refined to R-factors of 21% or better. The crystallographic parameters are listed in Table I below. The crystals were flash-frozen in liquid propane using 5-30% glycerol and maintained at –175 °C during the data collection. X-ray diffraction was collected on an [[Raxis-IC]] Raxis-IV image plate with a rotating anode generator (Rigaku, Tokyo, Model RU300) using 1.54X radiation. The data were integrated and scaled using the program HKL2000 (Otwinowski, Z., Oscillation data reduction program, in Data Collection and Processing, L. Sawyer, N. Issacs, and S.W. Bailey, Editors. 1993, Science and Engineering Council/Daresbury Laboratory: Warrington, United Kingdom. p. 56-62.). The crystals all had the same space group and cell dimensions as the native p38 crystals. The difference electron-density maps were calculated using the phases from the native p38 coordinates. The compounds were modified in Insight II from similar molecules obtained from the protein data bank {indomethicin for sulindac sulfide; and quercetin (3,5,6,3',4'-pentahydroxy flavone) for PD98059. ~~The corresponding protein data bank access codes are 4COX and 2HCK, respectively.~~ These molecules were then fit into the electron density using the program O (Jones et al., 1991, *Acta Crystallogr. A* 47:110-119). Positional and B-factor refinements were carried out using X-PLOR (Brunger x-PLOR: A system for x-ray crystallography and NMR (Yale University, Dept. of Molecular Biophysics, New Haven, CT

Version 3.85) and model building was done using the program O (Jones et al., 1991, *Acta Crystallogr. A* 47:110-119). Bulk solvent correction was applied at the final stage of refinement in X-PLOR. The backbone conformation of at least 80% of the amino acids is within the most favored regions of the Ramachandran plot with none in the disallowed regions as defined using the program PROCHECK (Laskowski et. Al. J. Appl. Crystallography 26 283-291 (1993)).

Please **replace** paragraph [00064] at page 37 with the following paragraph:

[00064] Binding site for sulindac sulfide and PD98059: The binding site in p38 for sulindac sulfide and PD98059 is at the hinge point between the two kinase domains. It is walled by the linker L5 (residues 76-83) that joins helix C (residues 63-75) with β4 (residues 84-89), the crossover connection (L7) (residues 106-109) and the C-terminus (βL16) (residues 310-336) (Figure 5). This site is outside the catalytic site Figure 4 shows the positions of the sulindac sulfide and PD98059 binding site of the present invention along with the ~~the~~ native ATP-competitive inhibitor binding site.